<u>REMARKS</u>

Claims 15-25 and 27-42 are pending in this application. Claim 26 has been canceled and claims 39-42 withdrawn from consideration. The claims have been amended as indicated above and support for the amendments can be found in the original specification.

Election/Restriction

Applicant notes with appreciation the withdrawal of the restriction requirement with respect to Groups I-V and examination of the claims in these Groups. Applicant also acknowledges the finality of the restriction requirement with respect to the claims in Group VI.

Rejection Under 35 U.S.C. § 102

Claims 15-16, 21, 23, 25-28, 34-36, and 38 have been rejected under 35 U.S.C. § 102(e) as being anticipated by Mangin (U.S. Pub No. 2003/0206864) for the reasons noted on page 3 of the Office Action. Applicant respectfully traverses this rejection.

Claims 15-25 and 27-33 contain the limitation of an ultrasonic radiation micro-bubble reagent that consists essentially of microbubbles, a carrier, and optionally a marking isotope combined with a targeting substance. And claims 34-38 contain the limitation of a medical device that contains an ultrasonic treating portion. The Office, however, has failed to show that Mangin teaches or suggests either of these claim limitations.

As to claims 15-25 and 27-33, Mangin discloses providing particles, agents or compositions for embolization. The particles, agents or compositions comprise particles which are used for embolizing vessels or ducts. The voids within, on the surface of, or between the

particles contain gas or microbubbles of gas so that the particle is visible under ultrasound. The embolic particle is introduced by injection and may be of various sizes that are large to cause embolization. The embolic particle is made of the material selected from the group consisting of silicone, polyester, vinyl polymer, fibrin, etc. *See Abstract and [0026-0027]*. But the current claims recite a reagent consisting essentially of microbubbles, a carrier, and optionally a marking isotope combined with a target substance, which would preclude the presence of particles in the claimed reagent.

Further, after the reagent is injected into a human body, ultrasonic radiation is used to irradiate the area where embolus is desired. The irradiation of such ultrasonic causes a cavitation effect of the microbubbles so that the blood vessel wall is broken up to introduce embolization of the blood vessel. *See [0032] of the present specification.* However, the ultrasonic component used in Margin just makes the particles visible since the energy is generally much lower. The micro-bubble reagent and ultrasound in the current claims interact with each other in a synergetic manner such that the embolization is increased significantly. *See [0041] of the present specification.*

Thus, unlike Mangin, the current claims recited a different micro-bubble reagent essentially free of particles. Under conditions of low energy and a low frequency ultrasound, a cavitation effect can be facilitated so as to break the blood vessel wall to cause embolization. Further, the marking isotope can be used to trace the micro-bubble reagent such that a SPECT equipment or Positron Electron Tracing (PET) can be used to detect the isotope and locate the tumor precisely, unlike Mangin where the voids containing gas or microbubbles of gas are used to make the particle visible under ultrasound.

As to claims 34-38, which contain the limitation of a medical device that contains an ultrasonic treating portion, the Office has not alleged—much less argued—that this limitation is described by Margin. There exists no mention in the Office's rejection of a device that contains an ultrasonic treating portion.

Thus, the Office has not shown that Mangin describes each and every limitation currently recited in the claims. Accordingly, Applicant respectfully requests withdrawal of this ground of rejection.

Rejection Under 35 U.S.C. § 103

Claims 17-20, 22, 24, and 37 have been rejected under 35 U.S.C. § 103 as being unpatentable over by Mangin for the reasons noted on page 4 of the Office Action. Applicant respectfully traverses this rejection.

The Office argues that Mangin discloses the invention substantially as claimed, but recognizes that Mangin does not describe the claimed irradiation frequency and timing or the reagent dosage. The Office argues that it would have been obvious to have used routine experimentation to determine optimum operating parameters to make the embolization process efficient and effective.

To begin with, the Office has not substantiated that all of these conditions are result-effective variables, which is required for the argument of obviousness via routine optimization. See M.P.E.P. 2144.05 (II)(B). Moreover, as noted above, the Office has not shown that Mangin discloses the claimed reagent. And the Office has not shown that the claimed reagent would have been obvious to the skilled artisan in light of Mangin's disclosure.

Accordingly, the Office has not substantiated a *prima facie* case of obviousness and Applicant respectfully requests withdrawal of this ground of rejection.

Rejection Under 35 U.S.C. § 103

Claims 29-30 have been rejected under 35 U.S.C. § 103 as being unpatentable over by Mangin in view of Feril for the reasons noted on pages 4-5 of the Office Action. Applicant respectfully traverses this rejection.

The Office argues that Mangin discloses the invention substantially as claimed, but recognizes that Mangin does not describe producing the CO₂ based reagent by reacting an organic acid and NaHCO₃. The Office argues that Feril teaches such a feature and that it would have been obvious to have produced carbon dioxide using the teaching of Feril in the process of Mangin because Feril teaches one known manner of producing carbon dioxide microbubbles at an known concentration and Mangin required microbubbles.

To begin with, the Office has not substantiated why the skilled artisan would have selected that method of Feril to produce carbon dioxide microbubbles, as opposed to any other known method. Moreover, as noted above, the Office has not shown that Mangin discloses the claimed reagent. And the Office has not shown that the claimed reagent is taught or suggested by Feril. And since the Office has not shown that either reference teach or suggests such a feature, it would be difficult for the Office to show that their combination teaches or suggest such a feature.

Accordingly, the Office has not substantiated a *prima facie* case of obviousness over the cited references and Applicant respectfully requests withdrawal of this ground of rejection.

Rejection Under 35 U.S.C. § 103

Claims 31-33 have been rejected under 35 U.S.C. § 103 as being unpatentable over by Mangin in view of Kung for the reasons noted on page 5 of the Office Action. Applicant respectfully traverses this rejection.

The Office argues that Mangin discloses the invention substantially as claimed, but recognizes that Mangin does not describe a marking or tracing isotope combined with a targeting substance. The Office argues that Kung teaches such a feature and that it would have been obvious to modify Mangin to include the tracing isotope taught by Kung since this allows determining where the isotope is delivered.

As noted above, the Office has not shown that Mangin discloses the claimed reagent.

And the Office has not shown that the claimed reagent is taught or suggested by Kung. And since the Office has not shown that either reference teach or suggests such a feature, it would be difficult for the Office to show that their combination teaches or suggest such a feature.

Accordingly, the Office has not substantiated a *prima facie* case of obviousness over the cited references and Applicant respectfully requests withdrawal of this ground of rejection.

CONCLUSION

For the above reasons, Applicant respectfully requests the Office to withdraw the pending grounds of rejection and allow all of the pending claims.

If there is any fee due in connection with the filing of this Amendment, including a fee for any extension of time not accounted for above, please charge the fee to our Deposit Account No. 50-0843.

Serial No. 10/556,237 Attorney Docket No. 13589.0002

Respectfully Submitted,

By

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Reg. No. 39,481

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